
CTN 004:
**Motivational Enhancement Treatment to Improve Treatment Engagement and Outcome
in Individuals Seeking Treatment for Substance Abuse**

Lead Investigator: Kathleen M. Carroll, Ph.D.
Department of Psychiatry
VA CT Healthcare Center (151D)
950 Campbell Avenue
West Haven, CT 06516
Work Phone: (203) 937-3486 x7403
E-Mail: kathleen.carroll@yale.edu

Co-Investigators (listed alphabetically):

Samuel Ball, PhD, Yale University
Paul Crits-Christoph, Ph.D., University of Pennsylvania
Chris Farentinos, M.D., ChangePoint
Tom McLellan, Ph.D., University of Pennsylvania
Jon Morgenstern, PhD, Mt. Sinai Medical Center
Jeanne Obert, M.S., Matrix Institute
Doug Polcin, Ed.D., Haight Ashbury Free Clinics
George Woody, M.D., University of Pennsylvania

Project Coordinator: Bryce Libby, LCSW.
Advanced Behavioral Health
Middletown, Connecticut
BLibby@ABHCT.com

Project Training Director: Samuel Ball, PhD
Yale University

Project Statistician: Charla Nich, MS
Yale University

Project Data Manager: Tami Frankforter
Yale University

Lead Node Coordinator: Julie Matthews, Advanced Behavioral Health
Jmatthews@ABHCT.com

NIDA Collaborators: Lisa S. Onken, Ph.D., National Institute on Drug Abuse
Ivan Montoya, M.D., M.P.H., National Institute on Drug Abuse

Consultants: William R. Miller, PhD, University of New Mexico
Theresa Moyers, University of New Mexico

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Summary of Protocol Amendments since Version 5

1. Distinction between SAE and clinical deterioration, pages 10-11. Only participants who have clear worsening of psychiatric, medical, or substance use symptoms during protocol treatment and who require a more intensive form of treatment (e.g. inpatient, detoxification, or residential care) should be considered as ‘clinically deteriorated’ and withdrawn from the treatment arm of the protocol.
2. Deletion of supervisor monthly face-to-face or conference calls page 19.

Summary of Protocol Clarifications since Version 5

3. As determined by the Steering Committee, subject payments may vary across Nodes to take into account local IRB guidelines, as well as special circumstances and geographic differences across Nodes. The Lead Node should be informed of any changes in level of subject payments, and these will also require local IRB approval. See page 32.
4. To assess recent alcohol use, CTPs may use either breathalyzer readings OR saliva strips. See page 21.
5. Clarification of intensity and format of ongoing supervision, page 17.
6. Clarification of treatment involvement and follow-up, pages 10-11.

Summary of Protocol Corrections since Version 5

1. The HRBS is an interview, not a self report. See page 20 and Table 1.
2. The inclusion criteria of ‘current substance abuse’ is operationalized as ‘within the past 28 days’. This is now consistent with the inclusion/exclusion form. See page 7.

1. Significance

Early dropout, partial attendance and early relapse are common occurrences in most substance abuse treatment programs. Given that (1) the bulk of attrition occurs very early in treatment and (2) retention in treatment has been linked to better outcome in several studies (Ball & Ross, 1991; McLellan et al., 1994; Simpson et al., 1997), identifying effective, practical means of enhancing initial treatment engagement and outcome is an important target for the Clinical Trials Network.

This protocol is appropriate for the CTN because:

1. MET is applicable to a broad range of participants and CTPs.
2. Multiple trials of MET and closely related approaches with substance using populations have supported its efficacy and durability.
3. Provision of training in MET has been identified as attractive to CTP staffs.
4. The focus on brief treatments and initial treatment engagement will allow for the study to be completed comparatively rapidly (e.g., within 1 year). This offers the advantage of rapid dissemination of findings to the academic and clinical communities.
5. The design is simple, straightforward and likely to be feasible within a wide range of clinics.
6. This study would allow some preliminary evaluation of strategies for training CTP clinicians to implement manualized therapies.
7. This protocol would generate important data about the nature of 'standard treatment' as practiced in the various Nodes and CTPs and thus set the stage for future Network protocols using "standard treatment" as a comparison condition.

2. Rationale

Several recent studies have suggested the effectiveness of brief motivational approaches for enhancing engagement among drug abusing populations. For example, Saunders and colleagues (1995) reported that a single session of motivational interviewing for participants entering a methadone maintenance program had greater commitment to abstinence and fewer opioid-related problems over a 6-month follow up period. Both Swanson and colleagues (1999) and Martino and colleagues (2000) reported that a single session of motivational interviewing was associated with better treatment compliance and retention for dual-diagnosis participants compared with treatment as usual in inpatient and day treatment settings, respectively. A multisite trial of 450 marijuana-dependent participants found that 2 sessions of MET was significantly more effective than a delayed-treatment control condition in reducing marijuana use and related outcomes (Babor et al, 1999). A study conducted in a community treatment program found that a single session of MET, delivered by the CTPs staff members who received only brief (single day) training, doubled the rate of treatment initiation compared to the standard evaluation among drug-abusing parents referred to treatment through the child protection system (Carroll, Libby, Sheehan et al., 1999).

Motivational Enhancement Therapy (MET) has a high level of empirical support as an effective, durable treatment for alcohol use disorders and smoking (Bien, Miller & Tonigan, 1993; Babor, 1994; Project MATCH Research Group, 1997; Wilk et al., 1997). Given the comparatively high severity of drug abusing participants, it is unlikely that this typically brief (3-4 session) approach will be sufficient treatment for many treatment-seeking drug-dependent individuals. Instead, MET techniques might be integrated into the early (orientation/entry/stabilization) phase of drug abuse treatment as a strategy to enhance initial retention and outcome.

3. Study Objectives

Primary objectives:

- A. To evaluate the efficacy of MET, relative to standard treatment at the participating CTPs, in enhancing treatment engagement and retention as well as in reducing substance use.
- B. To evaluate the durability of MET relative to standard treatment at the CTPs through a 3-month follow-up.

Secondary objectives:

- A. To explore participant characteristics associated with outcome, as a preliminary step toward understanding the types of participants particularly suited for MET versus those for whom standard treatment is sufficient.
- B. To evaluate the ability of clinicians at the CTPs to learn and effectively implement MET techniques.
- C. To conduct process analyses which will seek to : (1) assess the discriminability and specificity of each of the treatment approaches, (2) evaluate process (e.g., therapeutic alliance, therapist adherence, therapist skill) and outcome (e.g., participant satisfaction level, participant motivation) measures that relate to successful treatment engagement, retention, and outcome, and (3) to characterize the nature of standard treatment provided at the participating CTPs.

4. Study Design

A. Overview of study design

This is a randomized, two arm study comparing individual MET to ‘standard treatment’ for individuals seeking substance abuse treatment. Participants seeking treatment at the participating CTPs will be randomly assigned to either ‘standard’ or “MET” treatment, with a 1- and 3-month follow-up. Primary outcome measures will include (1) treatment retention (e.g., number of weeks in treatment), and (2) substance use (e.g., days of substance use, as confirmed by urinalysis, during the treatment and follow-up period). Secondary outcomes will include motivation, psychosocial functioning, HIV risk behaviors, treatment utilization, and

participant satisfaction. Process assessments will include measures of the working alliance as well as therapist adherence and competence ratings.

This protocol is intended for CTPs where individuals seeking treatment receive several individual sessions as part of the early phase of treatment. Following initial assessment, participants will be randomized to either 3 sessions of individual standard treatment or 3 sessions of individual Motivational Enhancement Therapy.

B. Participating CTPs

1. CTP characteristics

CTPs participating in this protocol should:

- Deliver treatment in an outpatient, non-methadone-maintenance setting.
- Have adequate numbers of new patients seeking treatment to meet target recruitment goals (e.g., 100 participants per CTP, with 50 participants per group)
- Have at least 6 clinicians willing to participate in the protocol (e.g., 3 for MET, 3 for standard treatment)

2. Rationale for CTP selection

We are focusing on outpatient settings because these avoid the possible issues of treatment contamination that occur in inpatient settings and because the nature of the protocol may not be practical in many inpatient settings.

We are excluding methadone maintenance programs because, unlike outpatient programs where the bulk of attrition occurs early (e.g., in the first month of treatment), early engagement is typically not a major problem in methadone maintenance programs. Instead, attrition and noncompliance typically emerges as an issue much later within methadone maintenance programs (e.g., 3-6 months after the patient is stabilized on methadone. Thus, including methadone maintenance programs in this protocol would entail a somewhat different approach (where MET would be used to focus on enhancing compliance and in stabilized patients) and time frame.

Multiple therapists per condition at each site are needed: (1) to reduce disruptions to the protocol associated with therapist absences (e.g., vacations) or therapist turnover, (2) to reduce scheduling problems and hence delay in assigning participants to clinicians, (3) to reducing the likelihood and magnitude of potential therapist effects, and (4) to permit some exploratory analyses of participant outcome by therapist fidelity or competence levels.

C. Participants

1. Inclusion/exclusion criteria

Individuals will be eligible for the protocol who:

- a. Are seeking outpatient treatment for any substance use disorder **and has used any substance within the past 28 days.**
- b. Are 18 years of age or older.
- c. Are willing to participate in the protocol (e.g., to be randomized to treatment, be contacted for follow-up assessment, to have their sessions audiotaped).
- d. Are able to understand and provide written informed consent.

Individuals will be excluded who:

- a. Are not sufficiently medically or psychiatrically stable to participate in outpatient treatment.
- b. Are seeking detoxification only, methadone maintenance treatment or residential inpatient treatment.

2. Rationale for participant inclusion/exclusion criteria

Broad inclusion criteria are proposed to allow a highly diverse participant sample with a range of substance use and related problems. Participants should be willing and able to participate fully in the protocol (e.g., to accept assignment to either condition, to provide sufficient locator information for follow-up, to allow their treatment sessions to be taped for fidelity/process assessment and supervision). Participants mandated to treatment will be included providing requirements of the protocol and the treatments provided are not incompatible with the conditions of their parole/probation. Individuals who are not medically or psychiatrically stable (e.g., untreated psychotic disorders, current suicidal or homicidal intent) are excluded because of their need for immediate acute care. Such individuals could be re-evaluated once stabilized, providing stabilization (e.g., acute detoxification) is brief.

3. Feasibility

As of August 2000; six CTPs have committed to implementing this protocol in their clinics. Thus, estimated sample size for this protocol is 600; which, as noted in the section on statistical power below, is more than sufficient to address the specific aims.

D. Procedures

1. Initial screening and informed consent.

Individuals seeking outpatient treatment at each of the sites will be identified and referred to the research assistant (note that in some CTPs, the research assistant may do the initial triage and screening). The research assistant will explain the purpose of the study, answer questions, review the consent form, and obtain informed consent from interested individuals. An investigator or sub investigator should participate in this

process OR review all consent forms with the RA. If possible, during the same session, the RA will complete the pretreatment assessment battery (see below). Uninterested individuals will be referred immediately to appropriate treatment at the CTP or another agency

2. Initial assessment

The research assistant will collect all baseline information from the participant (see section on Assessments, below). The research assistant will then transfer some of the data collected from the baseline assessment to the Personal Feedback Report for those participants assigned to MET, as well as filling out the Session 1 worksheet for the therapist.

3. Randomization

To increase the likelihood that treatment groups are balanced with respect to demographic and key prognostic variables (e.g., gender, race, education, motivation, principal drug of abuse, whether individual was mandated to treatment), participants will be assigned to treatment conditions through urn randomization. In urn randomization, an algorithm modifies ongoing randomization probabilities based on prior composition of treatment groups, maximizing multivariate equivalence of treatment groups (Stout et al., 1994). Thus, urn randomization offers the benefits of balancing allocation of important prognostic variables in treatment groups, while still retaining other benefits of random assignment (Wei, 1978).

Operationalization of urn variables:

- Gender (male, female)
- Race (Caucasian, African American, Hispanic, Asian, Other)
- Primary drug of abuse (cocaine, methamphetamine, alcohol, opioids, marijuana, benzodiazepene, other) (from ASI lite)
- Mandated to treatment (yes, no)
- Employment status (yes, no)

Urn randomization will take place at the CTP using an Access program (or a comparable procedure using an identical mathematical algorithm) and be done by the research assistant. Data from a sample of 218 alcohol, cocaine, and other drug users in Dr. Jon Morgenstern's recent protocols indicates 88% concordance between participants 'declared' self-reported primary drug problem on the ASI (item 14a) and SCID symptom counts. Thus this item will be used as proxy for 'primary drug of abuse'.

4. Treatment phase

Treatment conditions are described in detail below. Study treatments will be delivered in 3 individual sessions in a time ‘window’ of 28 days from the point of randomization. During this time, participants will meet weekly with the clinical evaluator/research assistant for collection of urine and breath specimens, as well as completion of self-report and interview assessments. Participants assigned to either group may also participate in ‘regular program activities’ as is usual at the CTP (e.g., education or orientation groups, day treatment, intensive outpatient treatment) *provided at least 3 individual sessions are offered* (MET or standard treatment).

Participants will be encouraged to come for treatment and for the evaluation sessions as described in the protocol and the treatment manuals. It will be emphasized to participants during screening that even if they have a relapse they should come to all scheduled appointments. They will be discouraged from using illicit substances, but there will be no protocol-specified penalty for drug use or for missed sessions. Participants who miss scheduled sessions will be encouraged to reschedule them within the 28-day treatment ‘window’ from the day of randomization.

5. Serious Adverse Events

Serious Adverse Events, as defined by CTN policy, involve a participant’s hospitalization for any reason or a participant’s death. The SAE reporting form (see SOP) should be completed and forwarded to the Node PI, the Lead Node, and the NIDA Safety Officer within 24 hours of staff notification that an SAE has occurred, following current CTN policy on reporting of SAEs. Local IRBs must also be informed as per their policy.

Participants who experience significant clinical deterioration (e.g., for suicidal or homicide attempts or significant suicidal or homicidal ideation, significant cognitive or medical deterioration, or significantly increased substance use) during the ‘active’ phase of treatment, may require more intensive treatment than the protocol can provide (e.g., hospitalization). In such cases, participants may be regarded as symptomatic failures, withdrawn from the treatment arm of the study, and referred for appropriate treatment at an appropriate facility. *Individuals who experience SAE’s should still be interviewed at posttreatment and for follow-ups*

6. Termination and follow-up

a. At the end of the 28 day treatment period, all participants will be interviewed by the research assistant, who will complete posttreatment assessments as described below and offer HIV testing and counseling.

b. Follow-up interviews will be conducted 4 and 12 weeks after termination of study treatments (e.g., 8 and 16 weeks after randomization). Follow-up interviews will include the full posttreatment battery. A one-month follow-up is included to enhance rates of follow up by

contacting participants soon after treatment termination. Because the protocol is designed to focus on strategies for enhancing initial engagement and retention, a 12 week follow-up should be sufficient.

Treatment involvement and follow-up

The MET/MI protocols are using the intention-to-treat principle, that is, we will contact all participants for all follow-ups (posttreatment, FU1, FU2), regardless of their level of participation in study treatments. It may be helpful to remind participants that, even if they decide for some reason to drop out of treatment or not receive their sessions, we will still be interested in reaching them for follow-up interviews.

Thus, once a participant is randomized, that participant should be contacted for posttreatment interviews (28 days) and all follow-ups, even if they do not receive a single session of their study treatment (MET or standard treatment).

Also, in the MET protocol, partial involvement is permissible. That is, following randomization, participants have 28 days to receive their 3 sessions. If they only receive 0, 1, or 2 sessions prior to the 28-day point, the posttreatment assessment should still take place at that point as well as the week 9 and week 17 follow-ups.

E. Treatments

1. “Standard treatment” or “Treatment as usual”

Participants assigned to ‘standard treatment’ would receive three sessions of individual counseling as is usually provided at that CTP. Other than offering three weekly individual sessions, standard treatment would not be otherwise constrained or controlled. That is, if it is standard practice at a CTP for patients to attend weekly group sessions in addition to individual counseling, participants in both MET and standard treatment would do so (providing the total number of sessions was equal across conditions and included at least 3 individual sessions of MET or standard counseling). Clinicians providing standard treatment at the sites would meet regularly with a clinical supervisor to review participant progress.

As in the MET condition, all sessions will be audiotaped and a sample will be rated by independent evaluators blind to the participants’ treatment assignment for process assessment (see section on process assessment, below). These analyses will address issues such as treatment integrity (e.g., Were MET and standard treatment discriminable? Did overlap of key MET interventions occur in standard treatment? Was therapist skillfulness different across conditions?) and evaluation of treatment process (e.g., is level of the therapist skill or therapist adherence associated with retention and outcome).

2. Motivational Enhancement Therapy

Grounded in principles of motivational psychology as well as Prochaska and DiClemente's (1992) processes of change theory, Motivational Enhancement Therapy (Miller & Rollnick, 1991 (Miller et al., 1992) incorporates elements found in successful brief intervention strategies, summarized by the acronym FRAMES: **F**eedback regarding personal risk, negative consequences, or impairment related to substance use; **e**mphasis on personal **R**esponsibility to change; the provision of clear **A**dvice to change; presentation of a **M**enu of change options; an **E**mpathic therapist style; and facilitation of the patient's **S**elf-efficacy.

In MET, the clinician seeks to increase the participant's commitment to change their substance use by heightening their awareness of the personal consequences that have resulted from their substance use (e.g., "What bothers you about your substance use?"), expressing empathy ("It must have been difficult for you to come here today"), and avoiding resistance and argumentation ("What you decide to do about your substance use is up to you; if you're willing to go on with the evaluation, we can spend some time talking about how you see the consequences of changing versus not changing your substance use").

As described in the MET manual (Farentinos, Obert, & Woody, 2000), MET will consist of three carefully planned sessions, with the first session focused on reviewing an individualized Personal Feedback Report, and the second two focused on discussing plans for changing substance use. The Personal Feedback Report will make use of data provided by the participants in their baseline assessment to summarize their view of substance-related problems, consequences, and reasons for quitting.

Personal Feedback Report: A key intervention associated with MET is feedback on consequences of substance use. This occurs during an early MET session (1 or 2) through review of a Personal Feedback Report (PFR), which summarizes objective information (e.g., neuropsychological or liver function tests) and the participants' own view of substance use and consequences. Information on negative consequences of substance use will be drawn from the participants' baseline assessment (e.g., sections of the ASI, and the SIP) and summarized by the research assistant on the PFR.

F. Therapists and Training

Therapist selection, training, and supervision procedures will be based on those used in previous Stage II multisite behavioral therapy trials (e.g. Crits-Christoph et al., 1998; Carroll et al., 1994; Rounsaville et al, 1983; Woody et al., 1983), but modified to meet the special needs of the CTN. This will include a high level of attention to support and ongoing supervision to the therapists (Morgenstern et al., in press), as well as a Node-centered approach to training and supervision intended to foster greater durability of MET in the CTPs after the trial is completed.

1. Therapist selection

Clinicians will be individuals currently employed at participating CTPs who are interested in participating in the research protocol, and:

- Willing to learn a manualized version of MET and follow manual guidelines for the duration of the protocol.
- Willing to be randomly assigned to either the MET or Standard Treatment condition and participate in any initial and ‘refresher’ training sessions.
- Willing to have their sessions be audiotaped for review by clinical supervisor and adherence/ competence raters, attend regular supervision sessions, and complete process ratings (e.g., ratings of the therapeutic alliance and techniques used during sessions) for the duration of the protocol.
- Approved by the CTPs administrative/supervisory staff as appropriate for the study (e.g., sufficiently reliable, performs CTP duties competently).

Clinicians who have received credentialing as a MET trainer, have received formal MET training within the three months prior to protocol training, or who have served as MET therapists in a prior clinical trial can serve as on-site MET supervisors for this study (see F.3 below), but cannot *serve as a therapist in either condition*. Clinicians who have received a less formalized or recent exposure to MET or motivational interviewing can participate as therapists.

“Trainees” (such as social work interns, psychology interns, psychiatry residents) may, with permission of the Node Expert Trainer ‘sit in’ on the initial MET training or the post-protocol MET training that will be provided to therapists not randomized to MET. Whether trainees can serve as protocol therapist will be a Node decision, based on considerations such as the trainee’s expected term within the CTP (e.g., will he or she be assigned to the CTP for the full duration of the protocol, whether the trainee’s schedule affords the flexibility to be assigned protocol participants), whether the trainee has adequate prior clinical experience (a trainee who has very limited clinical experience would be inappropriate), and whether trainee participation might preclude participation by a long-term CTP staff clinician.

All clinicians who meet the criteria above and express interest in participating in this protocol will be randomly assigned to be trained to provide MET or standard treatment. Random assignment is necessary to insure that the MET condition is not implemented only by clinicians who are highly motivated for training and supervision (who consequently are likely to be more skilled) while standard treatment is delivered by clinicians with less interest or motivation.

To enhance the ‘buy-in’ of all CTP staff, it may be useful to provide the non-MET assigned clinicians and all CTP staff who have elected not to participate in this protocol (or whose CTP supervisor has not approved) some alternate form of psychosocial treatment training that does not overlap with MET and is unlikely to be part of a CTN study in the next two years (e.g., Stage I study treatments being conducted at RRTC). In addition, all clinicians who are randomly assigned to the Standard Treatment condition should be offered the MET

training once participant recruitment has been completed for this study. These clinicians would also then be eligible to serve as MET therapists if their CTP chooses to participate in subsequent MET protocols that might be conducted as part of the CTN.

2. **Therapist assessment**

Because a secondary aim of the project is to conduct a preliminary evaluation of therapist characteristics associated with ease versus difficulty in learning or implementing MET, a very brief assessment of the clinicians will be done. Although future CTN protocols may make more demands on therapists in this regard to answer more sophisticated questions (e.g., relation of therapist attitude, beliefs, and expectations), a highly intrusive assessment process may hinder the CTP buy-in process for this early CTN protocol.

Domains to be assessed **before the protocol** is initiated will include:

- Demographics (therapist gender, age, race),
- Training and Experience (years of experience in substance abuse, years at current CTP, education/degree, certification status, and primary therapeutic orientation).
- Pre-training Audiotape from the therapists to be assigned to each condition of a typical case seen by them at their CTP. One pre-training audiotape is necessary to establish a baseline from which the effects of training on practice during the protocol and after protocol (for both conditions) can be measured.
- Therapist Checklist (self-report version of adherence/competence rating form) to measure how therapists see themselves providing clinical care in general. The protocol clinical supervisor also will rate the pre-training audiotape provided on the Adherence/Competence rating form.
- Evaluation of Training.

Domains to be assessed following each session **during treatment** will include:

- Therapist Checklist (self-report version of adherence/competence rating form)

Domains assessed **once during each participant's treatment** include:

- Therapeutic Alliance

Domains to be assessed at **protocol completion** (and 4 and 12 weeks after termination of protocol supervision) will include:

- Post-protocol Audiotape from the therapists in each condition of a typical case seen by therapist at their CTP. A post-training audiotape is necessary to measure changes in clinical practice.
- Therapist Checklist (self-report version of adherence/competence rating form) to evaluate how therapists see themselves providing clinical care in general. The protocol clinical supervisor (and independent tape raters) also will rate the post-protocol audiotape provided on the Adherence/Competence rating form.
- Evaluation of Supervision.

2. Trainers and supervisors

a. Node MET/MI Trainer/Supervisor

1. Roles and responsibilities.

At each participating Node, a principal MET/MI trainer/supervisor will be identified. This individual should be an experienced clinician/supervisor who has extensive background in MET/MI or who has been specifically trained in training clinicians to perform MET/MI. In Nodes with several participating CTPs, two Node MET trainer/supervisors may be needed. The Node trainer/supervisor will be responsible for:

- Attending a centralized initial training/planning seminar ("training of trainers") with the other Node MET supervisors, the goal of which is to standardize training, supervision and tape rating procedures across Nodes.
- Providing initial didactic training to each of the therapists participating in this protocol at the Node. The Node supervisor will also be responsible for training new therapists as needed at the Node as well as 'refresher' trainings as needed.
- Training and supervising CTP MET supervisors.
- Rating a sample of MET/MI tapes from each therapist at the Node for adherence/competence while the study is ongoing to monitor quality control and foster greater consistency in treatment delivery across participating Nodes and CTPs.

2. Training of Node MET trainer/supervisors (e.g., "Training of Trainers")

"Training-of-trainers" will be centralized across CTN nodes and precede the training of the CTP supervisors and training of the therapists, which then will be provided locally within each node. "Training-the-trainer" will be provided by a national expert in MET (e.g., William Miller) and will consist of a two day meeting involving the Node MET Expert trainers. Because these trainers should already be highly experienced in MET, there will not be a need to do anything more than a refresher didactic session (e.g., no more than 1/2 day). The remainder of the meeting will be spent finalizing the training curriculum, treatment manuals and achieving consensus on a training approach to be used across the CTPs to train supervisors and therapists to provide MET as conceptualized within this research protocol. Nodes will have flexibility with regard to how many individuals to send to the centralized "training-the trainer" sessions.

Training of trainers will also include review of guidelines for supervision of MET and initial calibration of adherence/competence ratings (see below). During both the training and the main phase of the study, the Node MET supervisors will meet via conference call regularly to enhance uniformity of ratings, supervision, feedback, as well as to discuss issues arising in training 'community' clinicians to use MET.

Once the Node MET supervisor/trainers have been trained and equipped with the MET manuals and other training materials (videotapes, role plays, slides), they will then train at least one CTP staff member (the CTP MET supervisor), (preferably in a clinical leadership position) and at least two clinicians from each CTP who will serve as MET supervisors and therapists respectively. This local MET training of CTP staff will involve the equivalent of two full days of didactic material, review of videotapes, role-playing, and implementation issues specific to this MET protocol. Given the differing CTP staffing issues and geographical distances between CTPs, nodes will have flexibility in the staging of this training including its frequency/ duration and location. For example, some CTPs may prefer two 8-hour trainings, while others may prefer four 4-hour trainings. In addition, some nodes may prefer to have all participating CTP supervisors and therapists attend one centralized training, whereas other nodes may prefer to conduct the training separately at each CTP, or combine CTPs in closer proximity. The principal requirements are that each CTP supervisor and therapist must receive 16 hours of training and all CTPs within a Node must be trained within a one-month period if separate trainings are done at each CTP.

b. CTP MET/MI Supervisor

To foster greater durability of MET in the participating CTPs; supervisors at each participating CTP will be drawn from current clinical supervisory staff (e.g., clinical or unit directors). These individuals will be receiving extensive training in MET and in supervising therapists to implement MET/MI effectively. They will receive ongoing consultation and support from an identified Node MET supervisor. The CTP MET supervisor will be responsible for:

- Attending the initial didactic training of CTP supervisors, as well as the training offered to the MET therapists. This will include training in rating audiotapes for adherence and competence.
- Reviewing and rating, using the supervisor checklist, a sample of audiotapes from each therapist during therapist training/piloting and while the study is ongoing (at least one per week during the main phase of the study).
- Meeting with therapists conducting MET at their site on a regular basis to review progress and rating forms, identify areas of competence in delivering MET as well as those requiring more work. Excellent guidelines for conducting supervision in the context of a multisite behavioral trial are provided in Witte & Wilber (1997) chapter and other sources.

In cases where it is determined that the CTP supervisor cannot take on the regular supervisory responsibilities, some of those responsibilities may be taken on by the Node MET expert trainer (e.g., providing ongoing supervision and quality control via review of audiotapes).

3. Training of MET/MI therapists.

a. Didactic seminar

All MET/MI therapists will complete a 16-hour didactic seminar led by the Node MET expert which will include overview of the aims of the protocol and study procedures, extensive review of the MET/MI manual, and completion of several training and role play exercises play (detailed training procedures are described in the Node Expert's manual. This protocol will be adapted and expanded to address some anticipated variability across clinicians with respect to level of experience, primary therapeutic orientation, basic therapy skills, and so on.

Issues that present initial challenges for many therapists delivering manual-driven therapy in the context of clinical trial will also be reviewed (e.g., adhering to manual guidelines with a diverse study population, monitoring via audiotapes, guidelines for supervision, randomization, roles of research assistants versus therapists, time-limited nature of the approaches)

One day of the two full days of training will include a didactic seminar that will include an overview of the aims of the protocol and study procedures and extensive review of the MET manual and the theory and practice of motivational interviewing. The second full day will include completion of several training and role-play exercises based on the protocol developed by Dr. Miller and the Node MET Experts. This protocol will be adapted and expanded to address some anticipated variability across clinicians with respect to level of experience, primary therapeutic orientation, basic therapy skills, and so on. In addition to participating in the standard therapist training, the CTP MET supervisors will receive detailed guidelines and training for supervision from the Node MET trainer.

b. Supervised practice/training cases

Training and supervision of therapists for this research protocol should take into account the clinical realities of conducting training in real-world clinical settings. Thus, the gold standard for Stage II efficacy trials, which typically includes a lengthy training period followed by an extended piloting phase culminating in a formal certification process may not be practical within the CTPs. Moreover, because an important general aim of the CTN is understanding the processes that facilitate the most cost-effective methods of training and supervising real-world clinicians working in community settings, neither a prolonged training period nor a formal credentialing process are proposed in this early CTN protocol. Finally, a credentialing process that excludes potential therapists before the study begins would preclude a more complete analysis of training/supervision factors associated with individual differences in the extent and skill with which therapists adhere to a manualized treatment approach.

After training, each therapist will conduct practice/training cases under close supervision by both the Node MET trainer (by phone) and the CTP supervisor, both of whom will review audiotapes and rate the tape using the adherence/competence checklist. These training cases are essentially an opportunity for each clinician to practice MET under highly supportive conditions with close supervision. The goal of the training case is for therapists to learn to adapt their usual technique to conform to manual guidelines, to identify the 'boundaries' of the

treatment, practice new techniques with patients resembling those they will treat in the main phase of the study, and to establish goals for ongoing supervision. All taped sessions from the training cases also will be forwarded to an independent evaluator who will review and rate a portion of them for adherence and competence.

Clinicians who are judged as adhering to the MET manual at least minimally (for example, at least 'adequate' rating on half of the MET rating scale items) will begin receiving randomly assigned participants. Clinicians who do not meet this minimal threshold will be assigned an additional training case and receive continued close supervision. Clinicians who fail to meet these minimal criteria on the second case will be assigned additional training cases, with written guidelines suggesting specific areas for working more closely within manual guidelines.

It is expected that this very minimal criterion is unlikely to lead to many exclusions of willing clinicians. Clinicians who narrowly miss exclusion will be expected to continue regular (weekly or biweekly) individual supervision, in addition to the standard every other week group supervision) with the CTP MET supervisor until they have scored in at least the 'adequate' range on half of the MET rating scale for two consecutive participants. This criterion will be considered the standard for certification as a MET therapist. The number of training cases required to reach this standard will be one variable to be explored in process analyses.

c. Ongoing monitoring/quality control

Quality control of MET treatment provided by therapists will be maintained through regular supervisory meetings, review of audiotapes, and therapist self-monitoring of their behavior through Therapist Checklists. **During the main phase of the study, each CTP supervisor (or Node MET expert) must provide biweekly group supervision (this may take place in person or by phone) and may provide individual supervision at their discretion.** This supervision will include review of audiotapes and provide corrective feedback around the use of prescribed versus proscribed techniques from the MET manual. The on-site MET supervisor will receive at least once monthly consultation (phone or face-to-face) with the Node MET supervisor regarding supervisory issues.

All therapy sessions will be audiotaped and stored in locked cabinets by the Research Assistant at each CTP. The Node Project Coordinator will insure that on-site CTP supervisors review specific tapes for supervisory purposes and will also distribute a subsample of these tapes for independent tape raters who will complete an Adherence/Competence rating scale (see below). The Training Coordinator from each Node will work collaboratively with the Node Project Coordinator to obtain feedback from independent raters of adherence/competence (as coordinated by the CTN Quality/ Assurance subcommittee) and deliver feedback to the on-site supervisor about therapists who are experiencing difficulty competently adhering to the MET/MI manual.

When a supervisor determines that a therapist is deviating significantly from protocol, he or she will request that a consecutive series of tapes be independently reviewed in an expedited fashion. If this review determines that the therapist has drifted below the level of initial certification, then intensification of supervision will be provided. This supervision format will continue with intensified tape rating occurring until the original certification level has been reached.

5. Adherence/competence rating scales

Assessment of therapist adherence (how closely did the therapist follow the manual guidelines, what interventions were actually delivered to the participant) and competence (how skillfully did the therapist deliver the treatment) in clinical trials of behavioral treatments based on session tapes is generally done at two separate times, by two different types of raters, and for two highly different purposes:

1. *Quality control.* The purposes of these ratings are to monitor and enhance the quality of the treatment that is delivered to the participants in the protocol. Adherence and competence ratings are completed by a supervisor or other expert in the treatment (who is NOT blind to the condition being delivered). On the basis of these ratings, supportive, corrective feedback and suggestions regarding the therapists' implementation of the treatment are provided to the therapist as soon as possible. This type of review of session tapes is critical in preventing and correcting therapist 'drift' and assure that high quality treatment is delivered to participants.

2. *Assessment of treatment integrity.* The purpose of these ratings is to demonstrate or document that treatments being compared were actually different, or discriminable, from each other in expected ways. For example, in this study, we would expect that that 'key' MET interventions (or active ingredients) will be frequently seen in tapes of MET sessions but rarely were rarely done in standard treatment. This type of rating is typically done by independent raters who are blind to treatment assignment (and hence can not be done by supervisors, who are not blind as to the type of treatment the clinician is delivering).

Adherence and competence rating instruments have been adapted from existing, well-validated instruments. Several adherence and competence items to evaluate MET were drawn from those used in Project MATCH (Carroll et al., 1998). Items used to capture 'standard treatment' and interventions not compatible with MET were drawn from validated scales used in previous studies evaluating drug counseling (e.g., Barber et al., 1996) and other interventions likely to be found in 'standard treatment' as implemented at the CTPs (e.g., Carroll et al., 2000; Morgenstern et al., in press).

G. Assessments

1. Overview

Assessments will address the following domains: (1) screening and description of the study sample, (2) predictors of outcome, (3) detection of response to treatments, and (4) assessment of the treatment process. The assessment battery was developed with the following principles in mind:

- a. Brevity: It is important keep the time between recruitment, randomization and the first session to a minimum and to keep participant burden low, particularly with a very brief intervention. A ceiling of two hours total time for the pretreatment assessment has been adopted.
- b. Evaluation and operationalization of primary and key secondary measures
- c. Linkage with 'core' CTN assessment battery.
- d. MET-specific measures for Personal Feedback Report. Measures of intensity and consequences of substance use are included for preparation of the Personal Feedback report.

2. Substance use severity, consequences, and frequency

a. Type, frequency, and intensity of alcohol and illicit drug use will also be determined by **urine and breath specimens** collected pretreatment, weekly during treatment, posttreatment, at follow-up. All urine specimens will be collected under staff observation and/or using temperature controlled monitoring and screened for illicit opioids, benzyloecognine (a cocaine metabolite), amphetamines, methamphetamines, and benzodiazepenes using the method for urinalysis selected by the CTN Core Assessment Working Group (currently the Roche TestCup system), which has the added advantage of on-site analysis and may reduce the need to collect multiple samples for research and clinical purposes.

b. Severity of substance use and substance-related problems will also be measured by composite scores of the **Addiction Severity Index (ASI)** (McLellan et al., 1992). The ASI is the most widely-used instrument for assessment of substance use and related problems and its psychometric properties are well established (Cacciola et al., 1997).

c. Type and severity of DSM-IV substance use disorders will be assessed via the **Substance Dependence Severity Scale (SDSS)** (Miele et al., 2000). Similar to the SCID, the SDSS has the comparative advantage of providing a current severity rating of for each symptom (e.g., tolerance, withdrawal, inability to cut down) and so will allow evaluation of change in severity of dependence over time.

3. Psychiatric disorders and symptoms

The prognostic significance of concurrent psychopathology in substance dependent populations has been noted in several investigations (McLellan et al, 1983; Rounsaville et al., 1986, 1987; Woody et al., 1984, 1985) and may be particularly relevant to treatment response in the CTN,

given its emphasis on treatment outcome among diverse populations. A continuous rating of psychiatric severity will be available through use of **the Psychological Severity Composite Score of the ASI** (McLellan et al., 1992).

4. *Other domains*

a. Readiness for change

As the participant's motivation, or readiness for change, may be an important predictor of response to treatment and is particularly relevant to this protocol (Prochaska et al., 1992), the **University of Rhode Island Change Assessment**, (DiClemente & Hughes, 1990) which assesses the participant's current position regarding readiness for change (e.g., precontemplation, contemplation, commitment), will be administered pre- and posttreatment and at follow-up.

b. Consequences of use

To assess the participant's perception of the adverse consequences of their substance use, a short version of the **Short Inventory of Problems (SIP-R)**, will be administered before treatment and at follow-up. The SIP is modified from the Drinker Inventory of Consequences (**DrINC**) (Miller et al., 1995), for use with drug users. Its psychometric properties have been found to be acceptable in previous trials (Miller et al., 1995). This instrument, with the ASI, will form the foundation of the Personal Feedback report for MET.

c. Treatment attitudes and expectations

Greater congruence of participant's expectations of treatment and beliefs regarding the causes and nature of substance use with those of the treatment they receive may result in improved outcome over participants whose treatment expectations contrast with study treatment received (Hall et al., 1991). The Treatment Attitudes and Expectation form, a self-report of treatment attitudes, adapted from the NIMH TDCRP (Elkin et al., 1985), has been modified for use with drug dependent individuals.

d. HIV risk behaviors.

Baseline level of HIV risk behaviors and change in those behaviors during treatment will be assessed using **the HIV Risk Behavior Scale (HRBS)**, a 12 item **interview** adapted from Darke *et al.* (1991) that includes a question regarding participant's knowledge of HIV status.

5. *Assessment of Primary Outcomes* (retention in treatment and substance use)

a. Urine monitoring conducted weekly during treatment and at each participant contact at follow-up. Breathalyzer samples (**or, depending on Node preference, saliva strips**) will be collected at each weekly assessment meeting to monitor alcohol use.

b. Self-reports of substance use (marijuana, cocaine, alcohol, methamphetamine, benzodiazepenes, opioids, and other illicit drugs) will also be documented at each contact by the research assistant via the **Substance Use Calendar**. Similar to the Form-90, which has been shown to be a reliable and valid instrument for monitoring substance use and other outcomes in longitudinal studies (Miller & DelBoca, 1994), the Substance Use Calendar instrument assesses substance use on a daily basis and allows a flexible, continuous evaluation of substance use. It also allows for collection of data points for participants who miss evaluation sessions and thus prevents missing data and problems associated with gaps or overlap of datapoints. The use of the calendar format prompts participants to remember key dates.

c. Other information on substance use and substance-related impairment will be assessed at monthly intervals via the ASI (McLellan et al., 1992).

d. The follow-up interview will also include SDSS to assess effectiveness of the treatments with respect to substance use severity.

c. Other outcomes

i. **Participant Satisfaction:** At the end of treatment, a self-report form will be completed by all participants, with ratings of participant's satisfaction with treatment, the degree of change of their condition, and perception of helpful or harmful aspects of the treatments received. This has been adapted from forms used successfully in Project MATCH and the CSAT multisite marijuana treatment trial (Donovan et al., under review).

iv. Treatment compliance: Number and duration of scheduled treatment sessions and post-study treatment involvement after completion of study treatment will be monitored via the **Treatment Utilization/Health Services Form**.

Treatment compliance will also be monitored by the therapists using the **Therapist Session Report and Technique Checklist**, which documents events such major changes in the participant's condition, other clinically significant events, number of scheduled appointments not kept due to client no show or rescheduling, as well as the specific interventions (MET, drug counseling, other) delivered in a given session.

6. *Measures of Treatment Specificity*

In order to evaluate the specific effects of the different types of treatments being compared, we will assess aspects of treatment outcome that are theoretically likely to be differentially affected by the study treatments: For example, the specificity of MET, which is intended to increase participants motivation for change will be assessed through the University of Rhode Island Change Assessment (URICA).

7. *Process Assessments*

a Overview

Extensive assessments of the psychotherapeutic process are intended to: (a) evaluate the extent to which treatments were implemented as intended and the validity of the independent (treatment) variable was protected, through assessment of treatment discriminability, (b) therapist adherence and competence in performing the treatment, and (c) assess the patient-therapist relationship as well as the extent to which the nature of the therapeutic alliance and other aspects of the therapeutic process are related to outcome.

b. Integrity of the independent (treatment) variable

To assure the study treatments (MET versus standard treatment) are discriminable and delivered in a manner consistent with manual guidelines, all therapy sessions will be audiotaped and selected sessions (estimating one session from each participant) will be evaluated by raters who are blind to type of treatment received, using the adherence/competence rating scales described above, which have been adapted from validated instruments for assessing adherence and competence in delivering MET, supportive interventions, and other treatments in previous trials (e.g., Barber et al., 1996, 1997; Carroll et al., 1998, Carroll, Nich, Sifrey et al., 2000).

c. Therapeutic alliance

Defined by Bordin (1979) as consisting of agreement on goals, agreement on tasks, and development of bonds between therapist and participant, the therapeutic alliance has proven to be a promising variable for predicting outcome from psychotherapy for substance abuse (Connors, Carroll et al., 1997) and other disorders (Horvath & Luborsky, 1993). In this study the working alliance will be assessed through the revised Helping Alliance Questionnaire (HAQ-II, Luborsky et al., 1996), a well-validated measure of this construct, from both the therapist and participant perspectives, after the first session.

H. Data Management & Analysis

1. Data Management

The Node data management system should allow for continuous active data entry, in a manner that allows for collected data to be reviewed for timeliness, accuracy, uniqueness, completeness, and reliability. The system should allow for feedback from the Node Data Manager within a week of the collected information, affording the research assistant the opportunity to re-evaluate the client to remedy protocol discrepant data. The data management system will provide for regular reporting on accrual rates and other key study progress indicators by CTP to assure compliance with protocol objectives. In addition, the Node data management system should support research assistants through training and documentation of research methodology as well as form specific instructions and manuals. The Node data management system should allow for accessible data by creating data sets in a system readable by the data archivists, or easily transferable to the data archivists.

Data will be entered continuously and processed by the data manager immediately. The data will be checked regularly for missing, illogical, out of range, and inconsistent values; accuracy of key variables such as gender, age, race, treatment assignment, and therapist, as well as checks within and across fields for logical inconsistencies. All of these have been defined in the Data Dictionary, which has been distributed to Node Data Managers, with the CRFs for each instrument. Weekly status reports should be distributed back to the research assistants with problems encountered that will need correction and clarification. These status reports will be returned immediately to the data manager to ensure readily available clean data. The data will be updated frequently for transmission to NIDA.

A codebook (including general file sizes, file name, table descriptions, reference tables descriptions, original data dictionary, anomalies of data, any missing values) will be updated as the data is transmitted to NIDA. Other codebooks such as on going data corrections and clarification documentation; accrual, retention, and follow-up reports; will be maintained at the Node and forwarded to NIDA as indicated.

The Node data management will also support a permanent internal documentation system of the activity of all data files, including logs associated with the dates of transfer from CTPs, data set sample sizes, data set completion, errors identified and means of resolution, an explanation of anomalies, and a date of transfer to the CTN data warehouse.

2. Data Analysis

Outlined below is the general strategy for data analyses that will address determination of the relative efficacy of treatments, analysis of potential participant predictors of outcome, and process analyses. Notes: The MET (CTN0004) and MI (CTN0005) studies will be treated and analyzed as two independent protocols.

1. Determination of Treatment Outcomes

a. Data reduction

Primary outcome variables have been defined a priori to reduce the risk of Type I error. As there is no single recognized indicator of outcome in substance abuse treatment, supplementary analyses will evaluate reliability, validity, and relationships between outcome variables (e.g., between retention in treatment and frequency of drug use, between drug use and psychosocial outcomes). Other preparatory analyses will include examination of distributions of outcome variables, validation of randomization through comparison of key demographic and drug use variables across treatment groups both within and across CTPs, as well as analysis of correspondence of self reports and biological indicators of drug use.

Since many statistical models have an assumption of normal distribution (Glass & Hopkins, 1984), all primary outcome variables will be assessed for normality. Any dependent variable

found to violate the assumption of normality will be transformed to reduce skewness. Documentation of all transformations, including statistical program and rationale, will be archived in the central data repository.

Operationalization of primary outcome variables:

Retention: Weeks in treatment at CTP through 3-month follow up.

Substance use: Days of substance use, validated with urine and breath specimen results.

b. Evaluation of treatment effects

The proposed study follows a single factor, two cell design in which psychotherapy condition constitutes the primary independent variable. All analyses will be conducted on the sample of all participants randomized to treatment regardless of actual exposure to treatment to avoid bias associated with analyzing more compliant subsets (i.e., compliance bias), with data pooled across sites (CTPs). The primary means of assessing retention will be a survival analysis using "week of termination" as the dependent variable and treatment group as the independent variable, with the addition of site and site-by treatment terms to assess site effects. Survival analysis does not require normal distribution of the dependent variable. Additional tests may include simple ANOVAs with the dependent variables "session completed" with treatment group as the independent variable, with additional terms added to evaluate site and site by treatment interaction.

These same statistical models will be applied to the substance use outcome evaluation. In addition, longitudinal analyses involving repeated assessment of the same variable (such as frequency of drug use by week over a 4-week period) may be evaluated using random effect regression analyses (Bryk & Raudenbush, 1987), with treatment as the primary independent variable. Like ANOVA, the random effect regression model allows for use of many independent variables and interactions, with the additional benefit of modeling outcomes for all participants, regardless of whether there is missing data or data collected off schedule.

c. Adequacy of sample size

A conservative approach to sample size calculation has been adopted that will permit, in addition to addressing the primary aims, undertaking several exploratory analyses that can be uniquely addressed through the CTN or are special interest for the CTN: First, for example, given that significant site- or site by treatment interactions may be more likely in the CTN than in other Stage II multicenter studies (due to diversity in patient samples, therapists, and 'standard treatment'), we thought it advisable to have adequate power to conduct secondary within-site analyses, should significant site effects or interaction be detected through the principal analyses. Thus, the power calculations presented below are based on the most conservative case; that is, if the pooled analyses reveal significant site or site by treatment interactions, it may be necessary to have adequate power to conduct some within-site analyses

for the primary outcomes. These power calculations suggest that the estimated sample size will be adequate to detect moderate effects within sites.

Second, an important secondary aim of the protocols will be to conduct a series of analyses using therapist, rather than participant, as the unit of analyses (e.g., evaluating outcome as a function of therapist skill in delivering MET or MI, evaluating level of training needed for different types of therapists). Thus, there are clear advantages to having larger number of therapists treat a 'meaningful' number of participants that can only be achieved through a comparatively large sample.

Finally, a larger sample size will allow analyses which can take advantage of the anticipated diversity of participants in CTN protocols; for example, evaluating treatment response by particular patient characteristic of high interest to the CTPs and the clinical community (e.g., response by level of psychiatric severity, whether participants are mandated to treatment, and so on).

a. H1: MET will be more effective than standard treatment in engaging and retaining participants and in reducing substance use within treatment.

<u>Outcome Type</u>	<u>Var Type</u>	<u>Statistical Method</u>	<u>Est. Effect Size</u>	<u>Sample Size</u>
Engagement	categorical	chi-square	Genesis, .71	26
Retention	categorical	chi-square	Genesis, .37	95
Substance use	continuous	t-test	Wilk outpatient, .43	236
Substance use	continuous	t-test	Largelge .80	70

Thus, to detect significant effects in categorical outcomes (e.g., retention), based on estimates of effect size from available studies (Wilk et al., 1997; Carroll et al., 2000), power would be adequate (.95) given a sample size of 95 at each CTP, should the primary analysis indicate within-site analyses are necessary. To detect significant effects in continuous outcome measures (e.g., drug use by week), the sample size of 95 is sufficient to detect moderate-to-large (.80) effect sizes within CTPs, should within-site analyses be necessary. This is consistent with the effect size on MET compared with directive counseling on substance use outcomes in the Miller et al. (1993) study.

H2: MET will be more effective than standard treatment in fostering continued retention in treatment and in reducing substance use through the 1 and 3 month follow up.

<u>Outcome Type</u>	<u>Var Type</u>	<u>Statistical Method</u>	<u>Est. Effect Size</u>	<u>Necessary Sample Size</u>
Engage/drug use	continuous	t-test	Small (.20)	1084
Engage/drug use	continuous	t-test	Medium (.50)	176
Engage/drug use	continuous	t-test	Large (.80)	70
Engage/drug use	dichotomous	chi-square	Small (.10)	1300
Engage/drug use	dichotomous	chi-square	Medium (.30)	145
Engage/drug use	dichotomous	chi-square	Large (.50)	52

For the follow-up data, the sample would be adequate to detect medium to large effects.

Secondary Aims

Preliminary power calculations for analyses of participant predictor variables are as follows:

Outcome Type	Variable Type	Statistical Method	Est. Effect Size	Sample Size
Retention or Substance use	continuous	regression, 2 predictors	Medium (.15)	107
Retention or Substance use	continuous	regression, 2 predictors	Large (.35)	48
Retention or Substance use	continuous	regression, 5 predictors	Medium (.15)	138
Retention or Substance use	continuous	regression, 5 predictors	Large (.35)	63

Within CTPs, a sample size of 100 would be adequate to detect differences in up to 2 predictors with a medium effect size.

c. Analysis of treatment specificity and process variables

1. Treatment specificity:

Analysis of treatment specificity data (e.g. change in motivation for MET) will be done through random effects regression models for continuous variables with multiple data points and repeated measures ANOVA models for measures collected at pre- and post-treatment only.

2. Predictive analyses

A limited number of participant characteristics that may independently impact outcome within or across treatment groups will be identified a priori based on theory and publication. These variables will first be assessed for independence from one another, and then participant to evaluations of equality across treatment groups, nodes, and sites. Pearson product moment correlations of the participant characteristics with outcomes will be run both within and across outcomes. Finally, aptitude treatment interaction analyses will be run to evaluate the relationship between the participant characteristic and treatment (e.g., Smith & Sechrest, 1991).

3. Process analyses:

Using data obtained from the independent observer rating scale of the audiotaped psychotherapy sessions, several steps will be taken to establish the psychometric properties of the assessment. First, the raters will be evaluated for consistency by having the session raters observe and rate the same subset of at least 15% of the sessions. Intra-class correlation coefficients will then be run on each of the variables to assess reliability of the raters. Once rater reliability has been established (and/or less reliable items have been eliminated from the subscale), the factor structure of the intended subscales will be assessed using confirmatory factor analysis. Once factor/subscales have been shown to be valid (and/or less correlated items have been eliminated from the subscale), treatment discriminability will be evaluated first with simple t-tests of subscale scores by treatment group by week. The second, more precise evaluation of treatment discriminability involves running a multiple groups profile analysis

(Harris, 1985) to evaluate all possible systematic effects and interactions (therapist, session, site within node, node, treatment, session by treatment, site within node by treatment, node by treatment, session by node, etc.). This completes the psychometric component of the process analyses.

Finally, our general model for analyzing the impact of specific adherence and competence ratings for each treatment will be to evaluate the effect of measured treatment delivery on outcome. Tests will include simple regression models with the dependent variables "weeks completed" or "percent days abstinent" with treatment score as the independent variable.

3. Interim Analyses

This trial will not involve over 1000 participants, will not involve treatments of 6 months duration or longer, will not be measuring deaths or serious adverse events as an efficacy measure, or evaluate a behavioral intervention for which published information supporting efficacy in the treatment of the addiction under study is considered limited or inconsistent. Moreover, this protocol is not considered likely to provide evidence of "overwhelming efficacy" of one treatment over another. Accordingly, interim analysis of accumulating efficacy data by treatment assignment is not planned.

Rather, in accordance with the Data Safety Monitoring Board's SOP, presentation of primary and secondary efficacy outcome data and other data not intended to evaluate safety will be presented for all treatment groups combined, further broken down by study node and, if feasible, by CTP. No statistical penalty will be taken for this blinded interim analysis of efficacy data which will be conducted for the sole purpose of assessing the acceptability of safety results.

Adverse event data and other data intended for the monitoring of safety will be presented to the DSMB in an unblinded fashion. Since the trial is not considered to be powered to demonstrate statistically significant differences in adverse events or other safety outcomes, p-values will not be calculated for any differences observed unless specifically requested by members of the Board to assist in the evaluation of a potential safety concern. No adjustments will be made for the number of interim analyses in the final report.

Although interim analysis of efficacy data is not planned, the Board may feel that such analysis is necessary to permit proper evaluation of safety data. Should an unscheduled interim analysis of efficacy be necessary, the Board will specify the question, the analysis required, the critical values for a decision and the statistical procedures necessary to control the overall type 1 error at $p < 0.05$. A protocol amendment will be included in the DSMB report of the analysis describing necessary changes in the statistical plan that result from the analysis.

I. Regulatory and Reporting Requirements

a. IRB Approval

Prior to initiating the study, the Principal Investigator at each study site will obtain written IRB approval to conduct the study. Should changes to the study protocol become necessary, protocol amendments will be submitted in writing to the IRB by the investigator for IRB approval prior to implementation.

b. Informed Consent

All potential candidates for the study will be given a current copy of the Informed Consent Form to read. The investigator or sub-investigators will explain all aspects of the study in lay language and answer all of the candidate's questions regarding the study. If the candidate desires to participate in the study, s/he will be asked to sign the Informed Consent. No study procedure will be performed prior to signing Informed Consent. Participants who refuse to participate or who withdraw from the study will be treated without prejudice.

c. Clinical Monitoring

All investigators will allow representatives of NIDA to periodically audit, at mutually convenient times during and after the study, all CRFs and corresponding source documents for each participant. These monitoring visits provide the opportunity to evaluate the progress of the study and to inform NIDA of potential problems at the study sites. The monitors will assure that submitted data are accurate and in agreement with source documentation; verify that study treatments are properly provided, verify that participants' consent for study participation has been properly obtained and documented, and confirm that research participants entered into the study meet inclusion and exclusion criteria.

D STUDY DOCUMENTATION AND RECORDS RETENTION

Study documentation includes all case report forms, data correction forms, workbooks, source documents, monitoring logs and appointment schedules, sponsor-investigator correspondence, and signed protocol and amendments, Ethics or Institutional Review Committee correspondence and approved consent form and signed participant consent forms.

Source documents include all recordings of observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical research study. Whenever possible, the original recording of an observation should be retained as the source document; however, a photocopy is acceptable provided that it is a clear, legible, and exact duplication of the original document.

E. CONFIDENTIALITY

1. Confidentiality of Data

By signing this protocol the investigator affirms to NIDA that information furnished to the investigator by NIDA will be maintained in confidence and such information will be divulged

to the Institutional Review Board, Ethical Review Committee, or similar or expert committee; affiliated institution; and employees only under an appropriate understanding of confidentiality with such board or committee, affiliated institution and employees.

2. Confidentiality of Participant Records

By signing the protocol the investigator agrees that within local regulatory restrictions and ethical considerations NIDA or any regulatory agency may consult and/or copy study documents in order to verify case report form data.

Table 1: MET protocol: SCHEDULE OF CLINICAL ASSESSMENTS, SOURCE OF RATINGS

Instrument	Times done	Purpose/domain	Time estimate		Rater	When rated			
			Interv iew	Self-report		Pretx	Weekly (1x/week x 4)	Posttx 28 days	Follow-up 1 & 2
Inclusion/exclusion criteria (IEC)	1	Establish eligibility, document reasons for ineligibility			RA	x			
Demographic Form (DEM)	1	Characterize sample, obtain variables for urn randomization	5 min		RA	x			
Randomization form (RAN)	1	Urn randomization							
URICA	4	Motivation measure, predictor of outcome		5 min	P	x		x	x
Treatment Attitude & expectations (AEQ)	1	Predictor of outcome		5	P	x		x	
SDSS-LITE (SSS)	3	Diagnostic, characterize sample, prediction of outcome,	20		RA	x		x	X (Fup 2 only)
Urine monitoring (UMR)	7	Outcome measure	5		RA	x	x	x	x
Breathalyzer (ABR)	7	Outcome	2		RA	X	X	X	X
ASI 'lite' (ASIP, ASI F)	1,3	Baseline assessment/ outcome/component of Personal Feedback Report	25		RA	x		X	X
Substance use calendar (SUP, SUA, SUF, SUF2a, SUF2b)	1,1,1,1,1	Self report of frequency of substance use, treatment tracking	10		RA	x	x	x	x
HRBS (HRB)	4	HIV risk behaviors, component of PFR, secondary outcome	5		P	X		X	X
Short Inventory of Problems-R (SIP)	1	Personal Feedback Report for MET, secondary outcome		5	P	X		X	
Treatment Utilization TUA, TUF, TUF2	1,1,1	Treatment utilization, compliance, estimates for cost evaluations	5		RA	x		x	x
Posttx Attitudes & Expectations (PAE)	1	Satisfaction with treatment			P			x	
Client disposition (CDE)	1	Participant response and disposition, including Serious Adverse Events			RA			x	
Helping Alliance Questionnaire (HAQC, HAQT)	1,1	Treatment process, rating of therapeutic alliance			T, P		Session 2		
Adherence/competence Rating Scale (STR)	1/week S, 1/month E	Quality control of treatment delivery/Process rating system/treatment integrity			E, S & R versions		X		
Therapist Session Report & Technique Checklist (TSC)	3	Treatment process/quality control			T		x		
Time estimate of pretreatment battery, not including informed consent or other CTP intake/evaluation assessments			67 min	25 min					

Instruments in Blue are CTN Core Assessments

Note: RA=Research assistant, P=Participant, T=Therapist, S=Supervisor, R=Process rater, E=Node MET Expert

J. HUMAN SUBJECTS

1. Subjects

- a. Individuals will be eligible for the protocol who:
 1. Are seeking outpatient treatment for any substance use disorder.
 2. Are 18 years of age or older.
 3. Are willing to participate in the protocol (e.g., to be randomized to treatment, be contacted for follow-up assessment, to have their sessions audiotaped).
 4. Are able to understand and provide written informed consent.

- b. Individuals will be excluded who:
 1. Are not sufficiently medically or psychiatrically stable to participate in outpatient treatment
 2. Are seeking detoxification only, methadone maintenance or other opioid agonist treatment, or residential or inpatient treatment.

2. Consent Procedures

After routine screening, all participants will receive an explanation of the study, risks, benefits, treatments, procedures and options for alternative treatment by the research assistant. Participants will be asked to sign the consent form if they wish to participate following resolution of any questions and clear indication that the participants understand the nature of the study and the consent.

3. Risks

a. Psychotherapy

The treatment evaluated here, Motivational Enhancement Therapy (MET), has been used safely in multiple trials with a range of substance-using populations in the past. Psychological risks are minimal and not different from those of equivalent non-study psychotherapeutic interventions, including the comparison condition (standard treatment at the CTP). For each treatment condition, frequent monitoring (at least weekly) of the participant's clinical status by therapists and research staff will insure identification and withdrawal from the study of participants who show significant psychological or symptomatic deterioration. Women of child-bearing age will be included in the study, as there is no known negative interaction of psychotherapy with pregnancy.

b. Urine and Breath Specimen Collection

Urine and breath specimens are collected at each interview as measures of outcome and as safeguards to participants. They should add no risks other than those normally associated with these procedures.

c. Rating Scale and Questionnaires.

These are all non-invasive, should add no risk, and have been used without difficulty or any adverse events in similar, previous studies with substance-abusing populations. The major disadvantage is the time taken to complete them and we have made extensive efforts to minimize the length of time needed to complete the battery as well as its overlap with assessments routinely conducted at the participating CTPs. Past experience with these and closely related measures indicates that they are acceptable to participants. Careful efforts aimed at maintaining confidentiality have been effective in previous research, and only participants' code numbers will be recorded on the forms themselves to protect confidentiality.

d. Audiotaping of Therapy Sessions

Audiotaping of therapy sessions is necessary to assure that the therapists administer the study treatments within explicit manual guidelines and to evaluate the degree to which overlap between conditions occurs. To assure the confidentiality and protection of participants with respect to audiotaping, the following steps will be taken:

(1) Participants have the right to refuse audiotaping. Participants who consent to audiotaping will be informed that they have the right to stop taping at any time during any session. Participants also have the right, at any point during participation, to request that all existing tapes be erased.

(2) Each therapist will conduct the taping him/herself. All taping will take place in the office of the participating CTP.

(3) Each tape will be labeled with the participant's study identification number, the therapist's identification number, the CTP code, and the session number (e.g., 1-3) and the date.

(4) The therapist will then give the completed tape recording to the Project Coordinator. Tapes will be stored in locked files in secure research offices in the participating CTP.

(5) To evaluate treatment integrity (e.g., whether the therapists followed the manual guidelines) and discriminability (e.g., to what extent motivational interventions were present in the 'standard treatment'), it is necessary that a portion of all session tapes be rated for therapist adherence and competence. For these ratings, the tapes to be sent to the Lead Node Coordinating Center (LNCC) will be copied at the CTP by the research assistant, who label them only with an identifying code and forward them to the LNCC. The copy is necessary because one tape should remain at the CTP for review by the CTP or Node supervisor, and one must be sent to the centralized location for rating. The copy also provides an additional safeguard in rare instances of damage or loss through shipment. The research assistant at the LNCC will document that the tapes have been received by the CTP, and distribute the tapes to the tape raters. Following the completion of the ratings, the tapes will be destroyed at LNCC and the CTP coordinator will be notified that this has been done.

(6) Access to the audiotapes will be limited to the CTP supervisors and the specially trained tape raters, who will rate the tapes in order to evaluate therapist adherence and competence in implementing treatment. All ratings will be done in secure research offices.

(7) Upon completion of these ratings, the audiotapes will be destroyed at both sites (CTP and *centralized location*).

4. *Protection of Participants*

Confidentiality in regards to collected materials will be maintained via a numbered reference system maintained by the research assistant.. Participants' names will appear only on a consent form and "key" form kept by the Node project coordinator in a locked cabinet.. Participants will be withdrawn from the study if they show severe psychological or symptomatic deterioration if clinically necessary for ethical or safety purposes. Participants dropped from a study for these reasons or because they wish to withdraw from a study will be offered treatment as usual at the CTP.

To further safeguard confidentiality, we have received a Federal Certificate of Confidentiality. Participation in the study will involve no increased risk to participants beyond that which would be incurred through seeking and entering treatment at the participating CTP. Prospective participants will be informed that their decision to participate in the study or to drop out of the study will have no impact on their relationship with the CTP or their ability to obtain treatment at the CTP in the future.

5. *Potential Benefits*

Benefits to participants include significant psychotherapeutic exploration through the provision of study psychotherapies. All participants will be offered a material inducement for participation in study evaluations including \$10 for each assessment completed. The major potential benefit in this study is in reduction of substance use via the study treatments, which may, in turn, foster improvement in participants legal, medical, interpersonal, psychological and occupational functioning. ***Note that individual Nodes may determine the amount of financial incentive for completion of research instruments. The local IRB must be informed of any change in level of incentives and this should be forwarded to the lead node.***

6. *Risk/Benefit Ratio*

Purely psychotherapeutic approaches are standard treatment in the majority of participating CTPs and treatment centers in the US. The study psychotherapies carry minimal risks and are likely to be of benefit. The psychological and laboratory assessments also confer minimal risks and these are minimized through confidentiality procedures and the used of skilled personnel. We believe we have included adequate safeguards for participants to address the ethical questions, including exclusion of participants at significant risk for suicide, regular contacts with program staff and close monitoring of symptoms, procedures to withdraw from study treatments participants who show significant deterioration, and minimization of coercive aspects of treatment and research participation. Thus, the potential benefits for individuals and society at large are great; and the risk/benefit ratio appears favorable toward the proposed study treatments.

Sample consent form: Yale HIC format

CONSENT FOR PARTICIPATION IN A RESEARCH PROJECT
YALE UNIVERSITY DEPARTMENT OF PSYCHIATRY

**Name of CTP*

Invitation to Participate and Description of Project

You are invited to participate in a study of ways to increase treatment involvement for substance use. You have been offered this choice because it is our understanding that you are seeking treatment for a substance use problem at this clinic

In order to decide whether or not you wish to be a part of this research study you should know enough about its risks and benefits to make an informed judgment. This consent form gives you detailed information about the research study that a member of the research team will discuss with you. This discussion should go over all aspects of this research: its purpose, the procedures that will be performed, any risks of the procedures, possible benefits and possible alternative treatments. Once you understand the study, you will be asked if you wish to participate; if so, you will be asked to sign this form.

Description of Procedures

This study will last for 4 weeks. Each participant will be assigned to one of the two following treatments:

1). Standard individual drug counseling.

This is identical to the treatment you would normally receive at this clinic. It will include three individual weekly sessions that will focus (****describe in terms of Standard Treatment at the CTP, such as*) *on orienting you to the treatment program, teaching you important concepts of recovery, increasing your self-awareness of specific problems you may be experiencing related to your addiction and demonstrating new ways of coping with skills designed to fit your lifestyle.* You will also be asked to complete a brief questionnaire and to provide urine and breath specimens for drug and alcohol testing. Each weekly session will require about one hour.

OR

2). Motivational Enhancement Therapy

This therapy will also take place in three individual weekly sessions and will focus on reviewing what you see as problems associated with your substance use and developing a plan to

change your behavior. You will also be asked to complete a brief questionnaire and to provide urine and breath specimens for drug and alcohol testing. Each weekly session will require about one hour.

We will decide what treatment you will receive by random selection. This means that your treatment will be decided by luck of the draw and not selected deliberately because of any special characteristics or problems you have.

When you enter the study you will be interviewed by study staff and asked to fill out questionnaires and provide a urine and breath specimen for drug and alcohol testing. This will require about one and 1/2 hours. At the end of the four weeks you will be asked to fill out more questionnaires, provide a urine and breath specimen for drug and alcohol testing, and be interviewed again. At the end of this part of the study, you may continue treatment at this, or if you wish, be referred elsewhere or leave treatment.

We request your consent to audiotape the treatment sessions. This taping is being performed in order to make sure your therapist is carrying out the treatment properly. Members of the research team will review the audiotapes only. . You also have the right to stop taping at any time during the evaluation. You also have the right, at any point during participation, to request that all existing tapes be erased. Audiotapes will not be used for training or any other purpose and identification of tapes will be by code number only. Following review of the audiotapes by members of the research team, the tapes will be erased.

We will contact you one and three months after you leave the study and ask you to come in for a brief interview, to fill out questionnaires, and to provide a urine and breath specimen for drug and alcohol testing. This will take about an hour each time.

You will be paid \$10 for completing each of the assessments (pretreatment, each week during treatment, posttreatment, and each of the two follow-ups. Therefore, if you complete each assessment as scheduled, you would be paid a total of \$70.

We will ask you to provide the names and telephone numbers of several individuals in your life who are likely to know of your whereabouts in order to help us locate you for the follow-up interviews. These individuals will be contacted only if we cannot locate you directly first; we will ask them only about where we may contact you (we will not ask about drug use or other problems); and we will not reveal to your locators any information about this study or your participation in it.

Risks and Inconveniences

We can foresee no known risks to participating in this treatment. We would like you to tell us about any times you use alcohol or illegal drugs while you are in the study. It is not illegal to report past substance use. Also, we know that stopping substance abuse can be quite difficult. In order to be helpful to you we simply need to know about your substance use. The urine drug tests and the breathalyzer tests for alcohol enable us to be certain of our results. The

only way you might be dismissed from the study is if you repeatedly do not come to treatment. Your obligation to the study is to do your best to stop using drugs, to be honest about yourself and your problems and to be available at your appointment times for both the research assistant and your counselor.

Benefits

This program may help you control your drug use. However, there is no guarantee that you will benefit from participating in this program. There will be no charge for any evaluation you receive from the study. Further treatment will be arranged at the end of the study (at the end of the four weeks) if you wish. If this involves this clinic, you will be charged for subsequent treatment as is usual.

Economic Considerations

All evaluations you receive as part of this study are provided free of charge. You will be paid for the time it takes to complete assessments. If you attend all seven interviews as scheduled that you will receive a total of \$70.

Alternative Treatments

Should you decide not to participate in this study, you will be referred to the regular evaluation and intake procedures and be referred to treatment as is usual at this clinic.

Confidentiality

We will make every effort to insure your confidentiality. In all records of the study you will be identified only by a number. Your name will not appear in any publication or be released to anyone without your written consent. Participation in the study will involve no increased risk to you. However, you should understand that there is a risk that you will be recognized by other participants or staff involved in the study, but this is no greater than the usual risk of identification that occurs in our usual treatment in this clinic. If you find this risk unacceptable you should not sign this consent form.

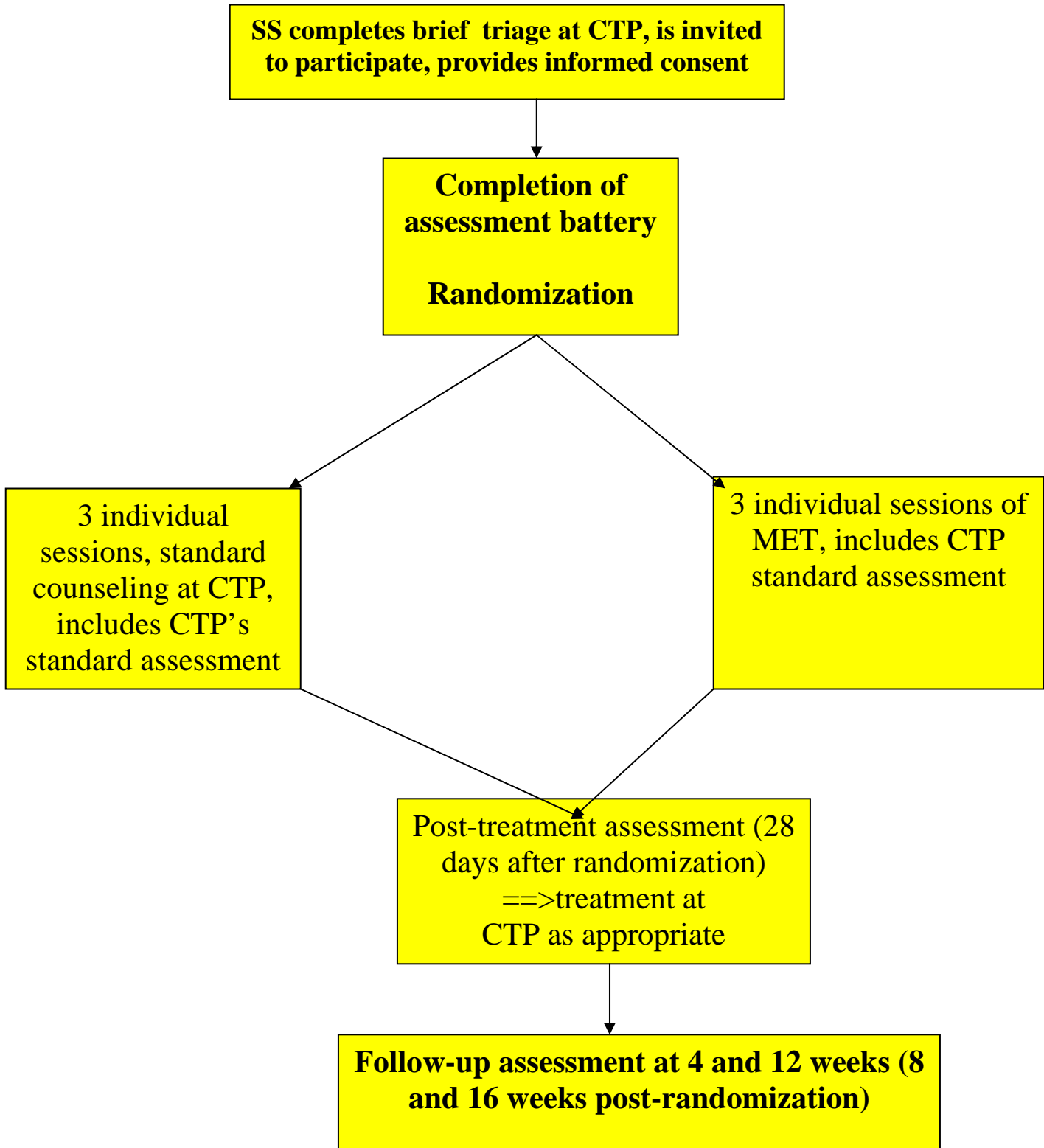
In order to further safeguard your confidentiality, we have applied for a Certificate of Confidentiality from the Secretary of the US Department of Health and Human Services. As a result, the investigators and anyone else involved in this project can not be compelled to reveal your name, urinalysis results, and other identifying characteristics to anyone without your written consent. This certificate protects investigators from being forced to release any research data in which you are identified, even under a court order or subpoena. This protection, however, is not absolute. It does not for apply to any state requirement to report certain communicable diseases, to report cases of physical or sexual abuse, or to disclosure of medical information in cases of medical necessity. These types of reports will not be made without your knowledge. The results of this research project may be presented at meetings or in publications; however, your identity will not be disclosed in these presentations.

Voluntary Participation

You are free to choose not to participate, and if you do become a participant, you are free to withdraw from the study at any time. If you withdraw it will not adversely affect your relationship with this clinic or the clinicians or doctors here. If you decide to withdraw, arrangements will be made with you to receive further treatment as needed.

Please feel free to ask about anything you do not understand and please consider this research and the consent form carefully before you decide whether or not to participate. You may take as much time as necessary to think it over.

MET protocol: Does incorporating MET into the treatment entry process enhance engagement, retention, outcome?



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